

## LETTER TO THE EDITOR

# Plasma fibrin clot structure and risk of thrombosis in rheumatoid arthritis

**Corresponding author** Prof. Anetta Undas, MD, PhD, Instytut Kardiologii, Uniwersytet, Jagielloński, Collegium Medicum, ul. Prądnicka 80, 31-202 Kraków, Poland, phone: +48 12 614 30 04, email: mmundas@cyfkr.edu.pl

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**Authors' reply** Thank you for your valuable comment. Our review of December 2017 focused on recent observations regarding altered fibrin clot phenotype associated with thromboembolic events, including myocardial infarction, stroke, and venous thromboembolism.<sup>1</sup> In patients with systemic inflammatory diseases, such as rheumatoid arthritis (RA) as well as chronic obstructive pulmonary disease (COPD), a prothrombotic state involving reduced clot permeability and prolonged lysis time has been shown to be associated with disease activity.<sup>2,3</sup> One might speculate that such prothrombotic fibrin clot phenotype contributes to the elevated risk of thrombosis in patients with active RA. However, to what extent altered fibrin clot structure and function may increase the risk of arterial and venous thrombosis in RA remains to be established in large prospective studies. Such impact of fibrin variables has been shown for recurrent venous thromboembolism during follow-up.<sup>4</sup>

Although many antiplatelet, anticoagulant, or cholesterol-lowering agents have been shown to favorably modulate fibrin properties,<sup>1,2</sup> the influence of steroids or specific antibodies (ie, infliximab) on fibrin clot phenotype, especially in patients with systemic inflammatory diseases, is unknown. Growing evidence indicates that the treatment with anti-tumor necrosis factor  $\alpha$  antibodies can suppress blood coagulation.<sup>3</sup> Similarly, patients with RA treated with tocilizumab, an interleukin-6 receptor inhibitor, showed a reduction in the levels of inflammatory markers, followed by a decrease in prothrombin fragment F1+2 and D-dimer levels.<sup>5</sup> This suggests that immunothrombosis is involved in RA-induced thrombosis, but the role of fibrin properties is unclear in this context. Therefore, we absolutely agree that further studies of patients with RA, with long-term follow-up, and with thromboembolic events as primary endpoints are warranted.

**Author names and affiliations** Michał Zabczyk, Anetta Undas: Institute of Cardiology, Jagiellonian University School of Medicine, John Paul II Hospital, Kraków, Poland

**Conflict of interest** The authors declare no conflict of interest.

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